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Case Report

A Case of Successful Treatment with an Immune Checkpoint Inhibitor after Head and Neck Photoimmunotherapy

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Keywords
Head and neck photoimmunotherapy · Head and neck cancer · Immune checkpoint inhibitor

Abstract
Introduction: Head and neck photoimmunotherapy (HN-PIT) has been conditionally approved by the Japanese government for the treatment of unresectable locally advanced or locally recurrent head and neck cancer since January 2021. HN-PIT makes local treatment of locally recurrent disease possible in cases where systemic drug therapy would have previously been the only option. However, when treatment is ineffective and the disease progresses, it is necessary to shift to conventional drug therapies. We report a case in which an immune checkpoint inhibitor (ICI) was successfully administered to a patient with advanced disease following HN-PIT. ***Case Presentation:*** A 75-year-old male patient presented with local recurrence of mandibular gingival cancer. The primary treatment consisted of mandibular segmentectomy and reconstruction with a scapulohumeral and vastus lateralis skin valve. Post-operative radiotherapy was administered. Local recurrence was found in the mid-pharynx adjacent to the reconstruction. HN-PIT was performed for the local recurrence. After three cycles of HN-PIT, the local lesion increased, and the disease was evaluated as advanced. Therefore, the patient was switched to pembrolizumab, an ICI. ***Conclusion:*** The recurrent lesions disappeared 2 months after the first dose of pembrolizumab, and the patient remained in clinical remission at 1 year. To the best of our knowledge, there are no other reports of successful ICI therapy after HN-PIT.

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Introduction

Head and neck photoimmunotherapy (HN-PIT) is a treatment in which cetuximab sarotalocan sodium is administered followed by irradiation with red light at 690 nm to specifically destroy tumor cells [1–3]. HN-PIT is performed for unresectable locally advanced head and neck cancers after standard therapies, such as surgery and radiation therapy, or for locally recurrent head and neck cancers that are difficult to treat. HN-PIT offers a local treatment option for patients who would otherwise require systemic drug therapy.

Since HN-PIT became available in Japan in January 2021, there have been few reports on its efficacy in actual clinical practice [4–9]. We report a case in which a patient with local disease that had progressed after three cycles of HN-PIT had a successful response to pembrolizumab, an immune checkpoint inhibitor (ICI) therapy.

Case Report

A 75-year-old male presented with recurrent mandibular gingival cancer. The patient was previously diagnosed with left mandibular gingival cancer (T4aN0M0, stage 4, squamous cell carcinoma) and underwent left mandibular segmentectomy, neck dissection, and reconstructive surgery using a scapular and vastus latissimus dorsi musculocutaneous flap. The patient underwent postoperative radiotherapy. One year and 3 months after radiotherapy, local recurrence was detected around the reconstructed area of the left middle pharynx. Computed tomography (CT), positron emission tomography-CT, and magnetic resonance imaging findings revealed no lesions other than a local recurrence. The target lesion was located in the lateral to posterior wall of the mesopharynx, adjacent to the reconstructed skin valve, and measured 33 mm × 22 mm (shown in Fig. 1). The recurrent lesion was distant from the internal carotid artery; therefore, HN-PIT was deemed appropriate. The patient's Eastern Cooperative Oncology Group performance status (ECOG PS) was zero and past medical history included partial resection of tongue cancer (T1N0M0, stage 1, squamous cell carcinoma).

HN-PIT Protocol

One day before laser irradiation, cetuximab sarotalocan sodium (640 mg/m^2) was administered intravenously over 2 h.

HN-PIT Cycle 1 in April 2022

The posterior wall of the middle pharynx was irradiated at four spots using a 20-mm cylindrical diffuser. The superficial lesions were irradiated using a frontal diffuser with a spot diameter of 30 mm. One month after HN-PIT, a CT scan showed that the recurrent lesions had reduced in size, but there was a residual tumor in the posterior wall of the pharynx.

HN-PIT Cycle 2 in June 2022

The residual superficial lesions were irradiated at four locations using a frontal diffuser with a spot diameter of 30 mm.

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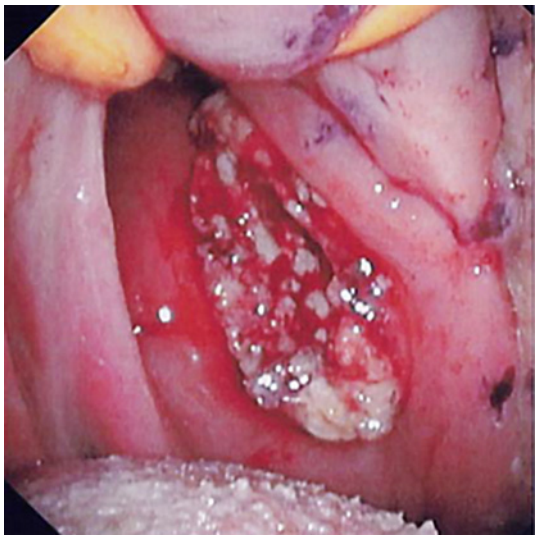

Fig. 1. An endoscopic view prior to head and neck photoimmunotherapy (HN-PIT).

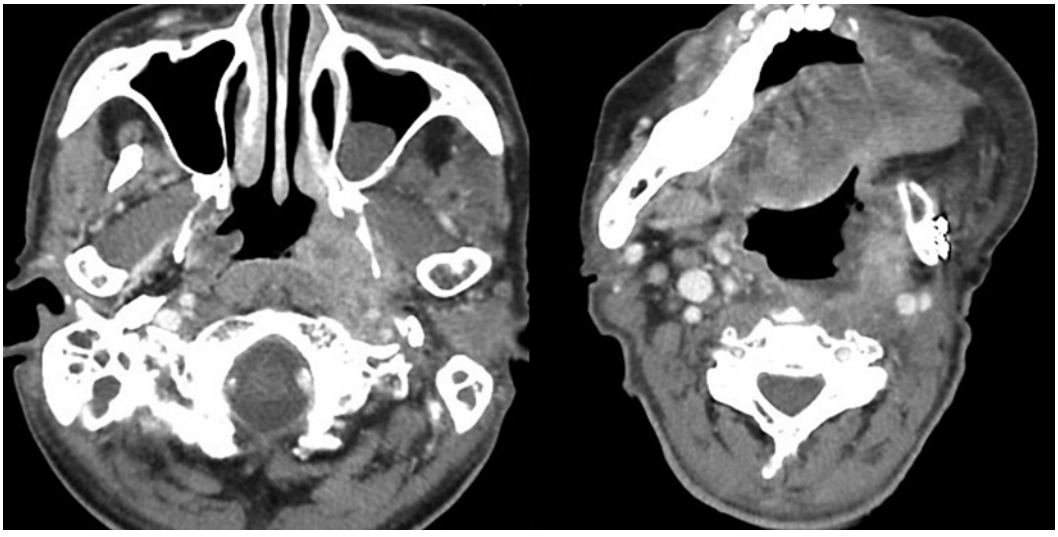

Fig. 2. CT images of disease progression after HN-PIT.

HN-PIT Cycle 3 in August 2022

Residual lesions were irradiated at six locations using 40-mm and 20-mm cylindrical diffusers. The superficial lesions were irradiated at two locations using frontal diffusers with spot diameters of 38 mm.

In October 2022, 6 months after the first cycle of HN-PIT, CT findings showed that the tumor had grown in the direction of the nasopharynx and masticatory muscle space and was considered progressive disease (shown in Fig. 2). The patient had no history of receiving platinum therapy, and his combined positive score was between 1 and 20.

Two months after the first dose of pembrolizumab, the recurrent lesions were no longer visible on CT scan (shown in Fig. 3a). No serious immune-related adverse events due to pembrolizumab were observed, and the ECOG PS returned to zero. Currently, in October 2023, more than 1 year after starting pembrolizumab, there has been no local recurrence (shown in Fig. 3b), and the patient continues to receive pembrolizumab.

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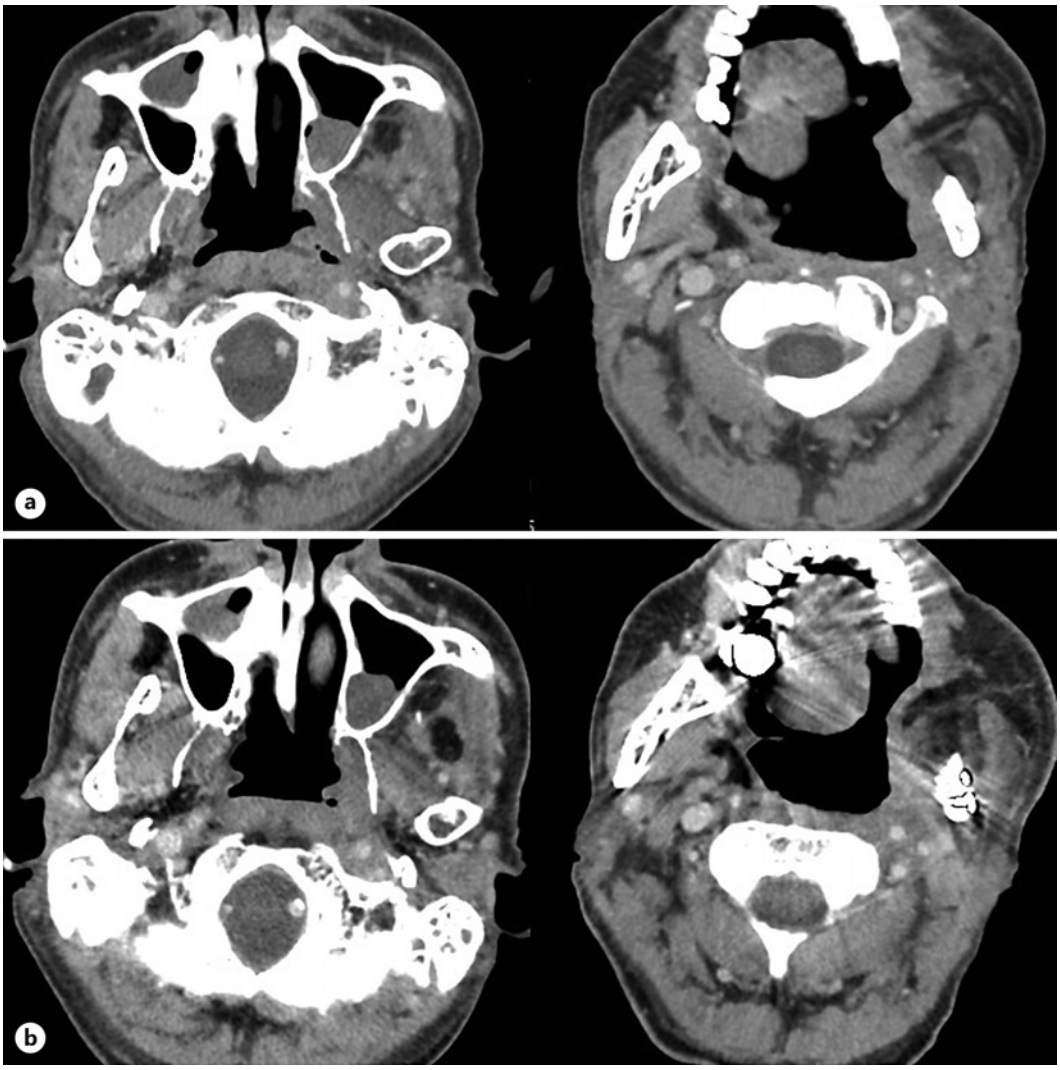

Fig. 3. a Computed tomography (CT) images 2 months after the first dose of pembrolizumab. **b** CT scan images 1 year after the first dose of pembrolizumab.

Discussion

Recently, the efficacy of nivolumab and pembrolizumab for recurrent metastatic head and neck cancer has been demonstrated [10, 11], and ICIs have become one of the mainstays of treatment of recurrent metastatic head and neck cancers. ICI has not only been demonstrated to be highly effective but also less toxic compared to pharmacotherapy. Consequently, it can be used to treat elderly patients and those with reduced ECOG PS, showing effectiveness in these groups [12].

The advent of HN-PIT has made local treatment an option for unresectable locally advanced and locally recurrent head and neck cancers where drug therapy was previously the only option. However, there have been only few reports on the treatment efficacy and adverse events of HN-PIT; thus, the evidence for the use of HN-PIT is limited. Further, whether to prioritize localized HN-PIT or systemic pharmacotherapy in unresectable locally advanced or locally recurrent head and neck cancers remains a consideration [13].

At our hospital, HN-PIT is performed whenever possible. There are two reasons for this: drug therapy administered prior to HN-PIT may preclude later use of HN-PIT when the disease progresses, and drug therapy is generally not a curative treatment, while HN-PIT can be curative. In cases where HN-PIT is not successful and the disease progresses, it is important to promptly shift to another treatment modality. Laboratory-based studies have shown that CD44-targeted PIT can improve the efficacy of anti-PD-1 ICI by increasing the number and density of activated CD8+ T cells in the tumor bed, thereby transforming less immunogenic tumors into more immunogenic tumors [14].

HN-PIT in combination with anti-PD-1 antibody therapy may enhance systemic anti-tumor immunity [15] because HN-PIT could improve host immunity on cancer antigen recognition and harvest additional multiclonal cytotoxic T cells. Therefore, the negative effects of HN-PIT on immunotherapy are likely minimal, and it may even have a positive effect. The treatment of recurrent metastatic head and neck cancers should continue to undergo clinical studies as a sequential therapy, taking into account both HN-PIT and ICI. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000536166).

Conclusion

The patient in this case study showed a complete response to pembrolizumab therapy after disease progression following HN-PIT for locally recurrent head and neck cancer. To the best of our knowledge, this is the first case report on the use of ICI therapy in this setting. These results suggest that immunotherapy may be an effective treatment following HN-PIT, and we hope that this case study will contribute to the development of an algorithm for the treatment of locally advanced or recurrent metastatic head and neck cancers.

Acknowledgments

We would like to thank the patient and his family for participating in this study. We would also like to thank our medical colleagues for their collaboration and contributions.

Statement of Ethics

The Ethics Committee of the Tokyo Medical University Hospital did not require ethics approval for this case report in accordance with national guidelines on retrospective reviews of patient data. Written informed consent was obtained from the patient for the publication of images and details of their medical case.

Conflict of Interest Statement

IO received lecturer fees from Rakuten Medical KK. The other authors have no conflicts of interest to declare.

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Author Contributions

K.H. and I.O. designed the study. K.H. wrote the manuscript and prepared the figures. I.O., K.To., and K.Ts. performed the photoimmunotherapy. All authors were responsible for the treatment of the patient. All authors discussed the results of the case report, commented on the manuscript, and approved the final version for publication.

Data Availability Statement

All data related to this case study have been included in this case report. Further inquiries can be directed to the corresponding author.

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